Synthetic Organic Chemicals

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The Preparation of Esters for Identifying Acids and Alcohols

THE use of esters in purifying and characterizing organic acids and alcohols or phenols is one of the most common and satisfactory methods. Although many of the reactions involving the formation of esters lead to equilibrium mixtures containing a low content of ester, there are numerous ways of making the yield substantially quantitative. Indeed, with the modern knowledge of ternary mixtures and the principles of distillation, most esterification procedures are quantitative. In characterizing an alcohol or an acid, however, one is generally working with small quantities and is unable to apply the methods used with larger amounts.

A Reagent for Acids

For acids, one of the smoothest methods of preparing methyl esters is through the use of diazomethane. This compound, a gas at ordinary temperature, is always employed in solution (ether, benzene, acetone, or occasionally, alcohol) and must be prepared shortly before use. The preparation may be (*1*) through the interaction of hydrazine hydrate, concentrated potassium hydroxide, and chloroform; (*2*) by the action of a strong methyl alcohol solution of potassium hydroxide on N-nitrosomethylurethane; or (*3*) by the reaction between 40% potassium hydroxide and N-nitrosomethylurea. Since the first method—hydrazine and chloroform—involves a rather elaborate generating apparatus, it is seldom used. The other two reactions are similar, and differ only in the ease with which each proceeds.

Nitrosomethylurethane is converted to diazomethane by refluxing it in the presence of ether with potassium hydroxide dissolved in methyl alcohol. The apparatus is so arranged that the ether and the diazomethane may be subsequently or continuously removed by distillation. The conversion of nitrosomethylurea to diazomethane proceeds more readily—so readily, in fact, that it generally is carried out with ice cooling. In this procedure it is only necessary to add the nitrosomethylurea to 40% potassium hydroxide which has been overlayered with ether, shake the mixture gently until no more gas development takes place in the aqueous layer, then remove the ether layer.

Stability of Diazomethane

In both cases, drying is effected by means of solid potassium hydroxide. The solution of diazomethane thus obtained is stable for some time, especially if stored at ice temperature. The strength of the solution is readily determined by means of an ether solution of benzoic acid. Since diazomethane is

poisonous, it should be used with suitable precautions. A method for the laboratory preparation of nitrosomethylurea can be obtained promptly on request to the Eastman Kodak Company.

Since methyl esters in the majority of cases are liquid rather than solid, the use of diazomethane as a reagent is limited. It has proved, however, to be of exceptional value in the investigation of acids of natural occurrence or formed through the breakdown of products of nature. For example, bilirubin, a compound of exceptional sensitivity toward acids, alkalies, and oxygen, can be methylated by means of diazomethane, whereas other methods lead to unworkable products. In rare instances diazoethane has been employed as a means of ethylation, but the difficulty of preparing the reagent is a serious handicap.

Para-nitrobenzyl Esters

For the majority of acids, esters satisfactory for use in identification are obtained by heating the sodium salt of the acid with p-nitrobenzyl bromide or p-bromphenacyl bromide. Through the investigations of E. Emmet Reid and his students, who have studied hundreds of these esters, very complete melting point data are available.

Alcohols are frequently converted into acetates, benzoates, or phthalates for purification; acetyl chloride, acetic anhydride, benzoyl chloride, or phthalic anhydride being generally used where the quantity is small. Phthalic anhydride in particular has recently found favor as a means of separating mixtures of the isomeric alcohols. The half esters formed by the reaction of this anhydride and alcohols are in many instances easily purified by crystallization. The method is limited, however, by the fact that the half esters often possess low melting points.

Under special circumstances it is sometimes desirable to use ketene as a means of acetylation. On account of the readiness with which it polymerizes, the ketene must always be prepared as used. It is conveniently made from anhydrous acetone by passing the vapor over a heated catalyst. The best of these appears to be vanadium pentoxide, especially when a considerable quantity is desired.

For small scale production the so-called ketene "lamps" are convenient. In these lamps the vapor of the acetone is brought into contact with hot wires of tungsten or platinum. A simple apparatus may be constructed from an ordinary 50-watt electric light bulb by sealing on suitable connections so that the excess acetone may be condensed and the ketene passed into the solution of the substance to be acetylated. As in the case of diazomethane, the cleanness of the reaction recommends the procedure. The apparatus is described by Ott, Schröter, and Packendorff in J. PRAKT. CHEM., (2), *130*, 177 (1931), and suggestions for its use are given in an article by Lipp and Koester in BER., *64*, 2824 (1931).

Dinitrobenzoates

The alcohol derivatives which have been investigated most thoroughly from the point of view of identification are the esters of 3,5-dinitrobenzoic acid. In the presence of pyridine, the reaction between 3,5-dinitrobenzoyl chloride and most alcohols proceeds rapidly and smoothly. Some of the esters so obtained, however, have melting points which are too low for convenient measurement. Further, in some cases the derivatives from alcohols boiling at substantially the same temperature have melting points which are so close together that definite characterization is impossible. In these cases solid urethanes may be formed with phenyl iso-cyanate, α-naphthyl iso-cyanate, or p-nitrophenylcarbamyl chloride.

Eastman Organic Chemicals as Analytical Reagents

XXVIII REAGENTS FOR SELENIUM AND TELLURIUM

HYDRAZINE HYDROCHLORIDE

Pellini and Spelta, GAZETTA *33*, 89 (1903)

In the reduction of selenium dioxide by hydrazine, one molecular weight of nitrogen is evolved for every atom of selenium reduced. The reaction is carried out in a suitable apparatus which provides for the collection of the nitrogen over boiled water. One gram of selenium dioxide yields 201.33 cc. of nitrogen, corrected to 0° C. and 760 mm.

The method is not satisfactory for tellurium dioxide as the evolution of nitrogen is too slow.

HYDRIODIC ACID

Moser and Miksch, MONAT. FÜR CHEMIE *44*, 361 (1923)

Hydriodic acid reduces selenium oxide to the elementary state but forms with tellurium, first the iodide and then a double salt. This difference permits the separation of the two elements, leaving the selenium in a weighable form, while the tellurium remains in the filtrate.

HYDROQUINONE

Putnam, Roberts, and Selchow, AM. J. SCIENCE *15*, 253 (1928)

This test, suitable for mineral analysis, consists in first dissolving the mineral grains in nitric acid which is later replaced by heating with concentrated sulfuric acid. After cooling to around 50-60° C., a drop of a saturated solution of hydroquinone in sulfuric acid is added, which gives the solution a yellowish brown color if selenium is present.

Tellurium is identified by the characteristic thin plates formed by evaporating the sulfuric acid solution of the mineral. Its presence can be further confirmed by adding a few drops of the hydroquinone solution and heating, which forms black needles or rods of elementary tellurium.

HYDROXYLAMINE HYDROCHLORIDE
HYDRAZINE HYDROCHLORIDE

Lehner and Kao, J. A. C. S. *47*, 2456 (1925)

Selenium can be separated from tellurium by reduction with hydroxylamine hydrochloride which precipitates the black, elemental selenium. Approximately one-half gram of the oxides is dissolved in 40 cc. of concentrated hydrochloric acid and diluted with water to 100 cc. The solution is then heated with 10 cc. of 25% hydroxylamine hydrochloride at 90° C. for 4 hours. The precipitate is filtered, washed with water and then with alcohol, dried, and weighed as Se.

Tellurium in the filtrate can be reduced by evaporating to 50 cc., adding 15 cc. of a saturated solution of sulfur dioxide, then 10 cc. of 15% hydrazine hydrochloride, and finally 25 cc. more of the sulfur dioxide solution. Boiling for 5 minutes precipitates the tellurium completely, after which it is washed and dried as above.

OXALIC ACID

Moser and Miksch, MONAT. FÜR CHEMIE, *44*, 353 (1923)

The warm alkaline solution of tellurous acid is treated with an excess of potassium permanganate and allowed to stand for a short time. The solution is then cooled sharply to 8° C. or 10° C. and acidified with dilute sulfuric acid. Tenth-normal oxalic acid is added in excess and after once more heating to 50° C. is back-titrated with potassium permanganate. The cooling before neutralizing the alkaline solution prevents decomposition of the permanganate during acidification.

New Eastman Organic Chemicals

	3373	Acetylmesitylene BP 126-128°/24 mm.	100 g.	$15.00	C
	3235	Alanine Ethyl Ester Hydrochloride MP 85-87°	100 g.	15.00	C
	1081	dl-Asparagine	100 g.	5.00	C
	3348	l-Benzoylalanine MP 142-144°	10 g.	10.00	A
P	3379	p-Benzylaminophenol (Practical) MP 84-85°	100 g.	10.00	C
	3319	Biuret MP 191-192°	10 g.	4.00	A
	3389	n-Butyl α-Hydroxy-iso-butyrate BP 64-65°/5 mm.	100 g.	5.00	C
	3401	n-Caproanilide MP 94-95°	100 g.	10.00	C
	3375	Cetyl Bromide MP 13-15°	100 g.	14.00	C
	3370	Cetyl Iodide MP 20-22°	100 g.	14.00	C
	3365	m-Chlorobromobenzene BP 81-82°/20 mm.	100 g.	6.00	C
P	3157	2.4-Diaminoanisole Hydrochloride 97-100%	100 g.	3.50	C
	3272	Dibenzanthracene MP 258-260°	1 g.	3.50	A
	3386	m-Diethylaminophenetole BP 134-135.5°/10 mm.	100 g.	12.00	C
	3420	3.5-Diiodo-4-hydroxybenzoic Acid MP 278-279° dec.	100 g.	9.00	C
	3364	4 4′-Dinitrodiphenylmethane MP 183-185°	100 g.	12.00	C
	2679	iso-Durene MP -26 to -24°	10 g.	6.00	A
	1430	Ethyl Fumarate BP 213-215°	500 g.	15.00	D
P	3395	Ethyl Furacrylate (Practical)	500 g.	16.00	D
P	3384	Ethyl Hydrogen Tetrachlorophthalate (Practical) MP 90-91°	100 g.	6.00	C
	3417	Glycerol Monomethyl Ether BP 111-114°/11 mm.	100 g.	6.00	C
	590	Glycogen	10 g.	7.00	A
	3388	n-Hexadecane MP 16-17°	10 g.	5.00	A
	3404	Histamine (Synthetic)	1 g.	4.00	O
T	596	Indene Fraction BP 165-175°	1 kg.	6.00	E
P	3394	Methyl Furacrylate (Practical) MP 21-24°	500 g.	11.00	D
	2080	Naphthoresorcinol MP 124-125°	10 g.	9.00	A
	3323	m-Nitrobenzonitrile MP 115-116°	10 g.	2.00	A
	3425	o-Nitrodiphenyl Ether BP 183-185°/8 mm.	100 g.	3.50	C
	3419	p-Nitrodiphenyl Ether MP 55-58°	100 g.	3.50	C
P	3398	m-Nitrohippuric Acid (Practical) MP 155-159°	100 g.	12.00	C
	3363	Nitromesitylene MP 43-44°	100 g.	15.00	C
	3410	α-iso-Nitrosopropiophenone MP 113-114°	100 g.	8.00	C
	3377	Phenoxyacetamide MP 101-102°	100 g.	10.00	C
	3414	Phenylethyl Sulfide BP 105-106°/30 mm.	100 g.	6.00	C
P	3380	N-Phenylglycine Potassium Salt (Practical)	1 kg.	2.50	E
	3405	Sodium 5-Nitro-6-chlorotoluene-3-sulfonate	100 g.	15.00	C
	3411	p.p′-Tetraethyldiaminodiphenylmethane MP 41-42°	100 g.	10.00	C
P	3399	Tetraethylene Glycol (Practical) BP 207-214°/20 mm.	500 g.	12.50	D